Approach to Acute renal failure

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Objectives :

- Definition of ARF .
- Epidemiology .
- Etiology of ARF .
- Management of ARF:
  - » Diagnosis of ARF
  - » Treatment of ARF

» Functions of the kidney are :

1. Excretion of waste products
2. Acid-base balance
3. Electrolyte balance

} These are important in Acute Renal Failure (ARF).

4. Hormonal (Erythropiotin secretion)
5. Regulation of vit. D
6. Regulation of blood pressure

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- **In ARF, there will be:**
  1. Accumulation in waste products (creatinine will be high) .
  2. Disturbed acid-base balance (they will have metabolic acidosis).
  3. Electrolyte imbalance (hyperkalemia, hyperphosphatemia and others)
- The hormonal function of the kidney will not be affected, because it is acute except if the pt stay in the acute renal failure for few weeks to months. And **vit. D** will not be affected as well. (It will take time)
- **What about blood pressure**?
  - It is usually not affected, unless if it ,hypotension, is the cause of ARF.

Acute Renal Failure (ARF) "the old name"

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Acute Kidney Injury (AKI) "the new name" :

- Deterioration of renal function over a period of hours to days, resulting in :
  - The failure of the kidney to excrete nitrogenous waste products, and
  - To maintain fluid and electrolyte homeostasis

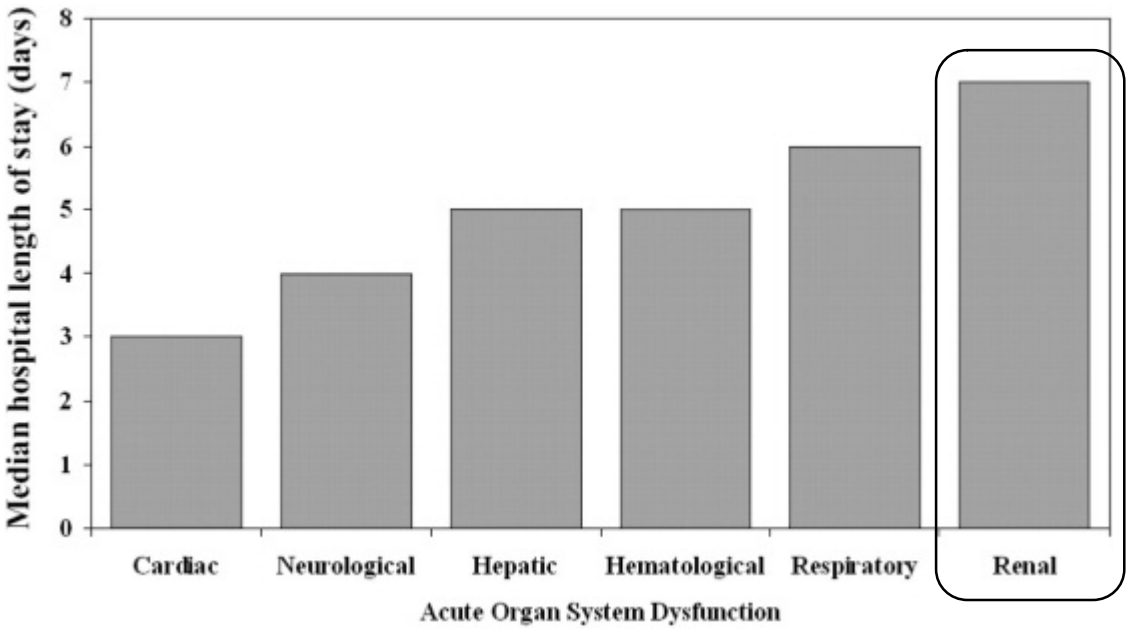
- ARF Rapid deterioration of renal function :
  - Increase of creatinine of **>0.5 mg/dl** in <72hrs.
    - *We don't use mg/dl here, we use the mol/l, which is equal to* **>44mol/l**.
  - Azotemia (accumulation of nitrogenous wastes).
  - Elevated BUN and creatinine levels.
  - Decreased urine output *(usually but not always)*

- **Oliguria** : <400 ml urine output in 24 hours.
- **Anutia** : <100 ml urine output in 24 hours.

• Epidemiology:

- It occurs in :
  - 5% of all hospitalized patients.
  - 35% of those in intensive care units:
    - *The incidence of ARF in ICU is high, because they are unstable pts.*
    - *They may have hypotension, severe diseases like sepsis, and others.*
  - Mortality is high:
    - Up to 75–90% in patients with sepsis.
    - 35–45% in those without.

Median hospital length of stay (LOS) stratified by single acute organ system dysfunction (AOSD), including acute renal failure (ARF).

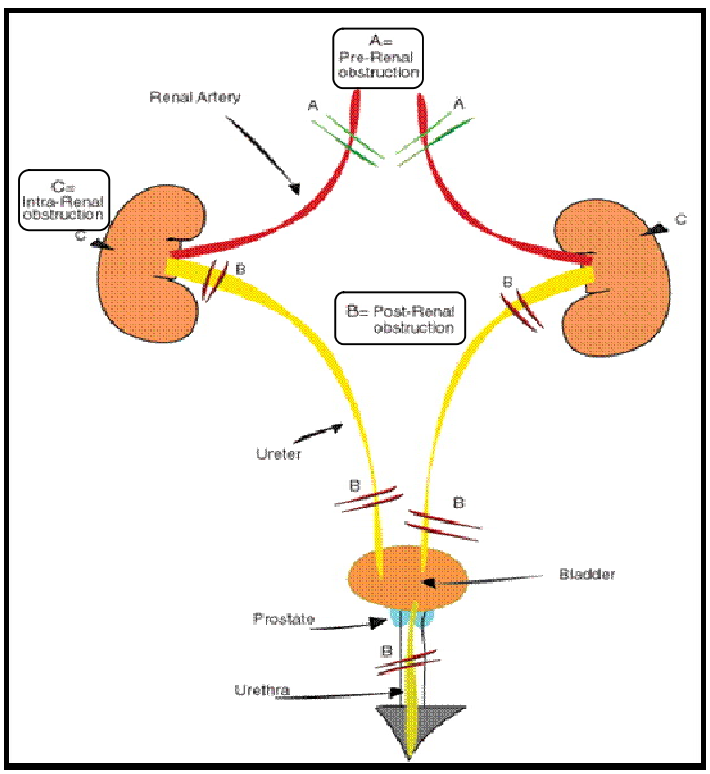


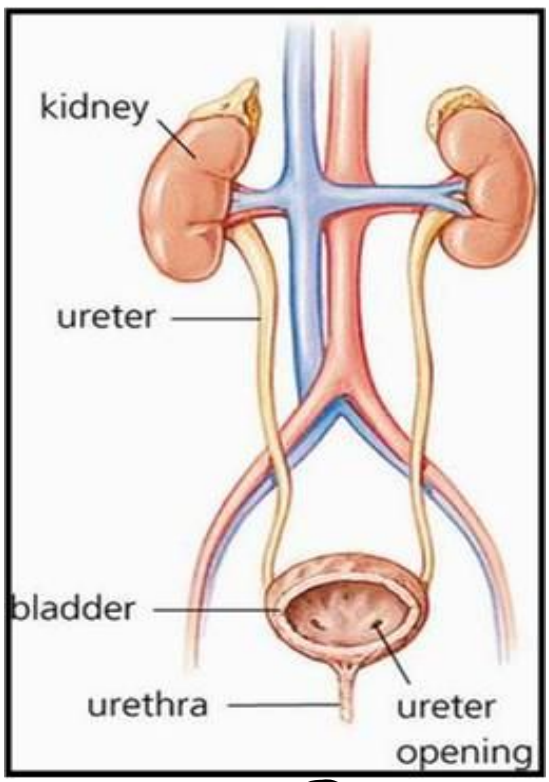
– *The hospital stay is longer. (the pts with renal failure stay longer than other pts) So, morbidity is high as the mortality is high, <u>that's why we care about ARF</u>.*

- Etiology of ARF:

We classify it according to the site of the problem to : <u>pre-renal</u>, <u>renal</u> (intrinsic), and <u>post-renal</u>, because it is easier to you in the **diagnosis** and the **treatment**.

The most common etiology is the pre-renal.





- Causes of acute renal failure :

1. ***Pre-renal AKI***

Any thing before the kidney, so the problem will be from the fluid or the blood or in the pump

- **Volume depletion :**

(Dehydration)

- Renal losses (diuretics, polyuria)
- GI losses (vomiting, diarrhea)
- Cutaneous losses (burns, Stevens-Johnson syndrome)
- Hemorrhage *(for any cause)*
- Pancreatitis.*(why pancreatitis? Because of fluid shifting to the third space)*

- **Decreased cardiac output :**

(25% of cardiac Output is going to the kidney, so, we need acute reduction of CO to cause ARF)

- Heart failure
- Pulmonary embolus
- Acute myocardial infarction *(ischemic heart disease)*
- Severe valvular heart disease
- Abdominal compartment syndrome (tense ascites) *rare*
- *Severe arrhythmias, but it is rarely cause ARF*
- *Temponade*
- *Severe cardiomyopathy*

2. Post-renal AKI

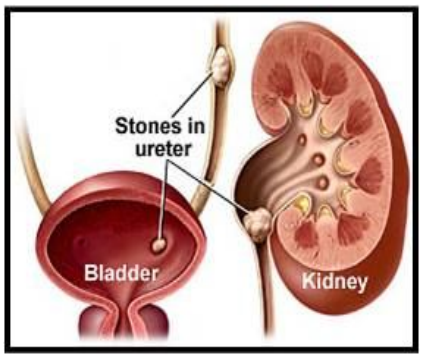
The cause is stone

- **Ureteric obstruction:**

If you have 2 functioning kidney, you must have obstruction for both ureters, bilateral obstruction, or the obstruction is in the nick of the bladder or the urethra to have ARF.

But when you have a solitary kidney or one abnormal or non functioning kidney, any obstruction to the ureter for the normal kidney will cause ARF

- Stone disease,
- Tumor, *(In the pelvis obstructing, the 2 ureters must be obstructed, "especially in female". e.g. uterine problem, ovarian, ...)*
- Fibrosis,
- Ligation during pelvic surgery



Bladder neck obstruction

- Benign prostatic hypertrophy [BPH]
- Cancer of the prostate
- Neurogenic bladder
- Drugs,
  - Tricyclic antidepressants, ganglion blockers
- Bladder tumor,
- Stone disease,
  - Hemorrhage/clot

Urethral obstruction

- Strictures,
- Tumor.

3. ***Renal***

If you take cross-section in the kidney you will see glomeruli, tubules, interstitial and blood vessels, so, the cause of renal ARF is one of these 4:

Glomerular

Glomerulonephritis can cause ARF but not any glomerulonephritis, it is Rapidly progressive glomerulonephritis that cause it, and we divided it into:

- Anti–glomerular basement membrane (GBM) disease
  - Goodpasture syndrome
- Anti–neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN)
  - Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis
- Immune complex GN
  - Lupus, post infectious, cryoglobulinemia, primary membrano-proliferative glomerulonephritis . *(post-streptococcal)*

Tubular

- Ischemic :
  - *Any pt with pre-renal cause, if you don't resuscitate him for a while , he will develop ischemia to the tubule (progression from pre-renal to renal), so you need to treat the pt in the pre-renal to prevent this progression.*

– Totoxic :

- Heme pigment (rhabdomyolysis, intravascular hemolysis)
- Crystals
  - Tumor lysis syndrome:

    > *After chemotherapy, the cells will lyse releasing K^+, uric acid, lipid. So, the pt will have hyperkalemia, hyperuricemia and hyperlipidemia and it will damage the kidney, so we have to give IV fluid to the pt*.

  - Seizures

    > *Muscle contraction and muscle spasm may cause muscle damage leading to release of heme pigment, which is toxic to the tubules as well as it will cause obstruction (Rhabdomyolysis)*.

  - Ethylene glycol poisoning,
  - Mega dose vitamin C,
  - Acyclovir, indinavir, methotrexate.
- Drugs
  - Aminoglycosides, lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, radiocontrast agents.

*(Acute tubular necrosis "**ATN** " is the most common cause of renal either ischemic or toxic)*

Interstitial

- *Mainly* Drugs :
  - penicillins, cephalosporins, NSAIDs, proton-pump inhibitors, allopurinol, rifampin, indinavir, mesalamine, sulfonamides and gold.
- Infection :
  - pyelonephritis, viral nephritides
- Systemic disease :
  - Sjogren syndrome, sarcoid, lupus, lymphoma, leukemia, tubule-nephritis, uveitis.

- Clinical feature :

  - Signs and symptoms resulting from loss of kidney function:
    - decreased or no urine output, flank pain, edema, hypertension, or discolored urine
  - Asymptomatic
    (Glomerular diseases may present with no symptoms)
    - elevations in the plasma creatinine
    - abnormalities on urinalysis
  - Symptoms and/or signs of renal failure:
    (due to elevated urea and creatinine)
    - weakness and
    - easy fatiguability (from anemia),
    - anorexia,
    - vomiting,
    - mental status changes,
    - Seizures, or
    - Edema.
  - Systemic symptoms and findings :
    (like if the pt has lupus or other disease, so the presentation could be for the disease itself and when you measure the urea and creatinine you will find it high):
    - Fever,
    - arthralgias,
    - pulmonary lesions

NB

- **How does the pt with ARF present?**
  - The symptom could be from the etiology or from the ARF itself.
  - E.g. If the pt has an car accident and his BP is low and when you measure the urea and creatinine and find it high, it is obvious that the pt has pre-renal ARF except if the injury is for the kidney.
  - If the pt presents with anuria with flank pain or is a known case of PBH, the cause might be post renal. *So, the history may give you a hint.*

- Diagnosis:

NB

- History is very important to differentiate between the pre-renal, renal or post-renal causes of ARF.
- Then, the examination: low JVP, low BP.
- For e.g.
  - Pt is tachycardic and in shock. So, the treatment is blood and IV fluid as pre-renal.
  - If the pt is obstructed, the treatment is to relieve obstruction.

- Blood urea nitrogen (BUN) and serum creatinine .
- CBC, peripheral smear, and serology .
- Urinalysis .
- Urine electrolytes
  - *It will be normal in post-renal because the kidneys still normal.*
  - *But in pre-renal and if the pt is hypotensive and dehydrated, the Na^+ will be low because the kidney still normal and the tubules will try to reabsorb the water and Na, and the urine will be concentrated high osmolarity,*
  - *In the renal if there is damage of tubules, Na will be high and the osmolarity will be low because of increased water secretion*
- U/S kidneys
  - *To role out obstruction and to see the size of the kidney,*
    - *if the size of the kidney is normal this is most likely acute, and*
    - *if it is small shrunken kidney it is most likely chronic.*
- Serology: ANA,ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobulin
- Urinalysis
  - Unremarkable in pre- and post-renal causes
  - Differentiates ATN vs. AIN. vs. AGN
    - **Muddy brown casts** in ATN *(acute tubular necrosis)*
    - **WBC casts** in AIN *(acute interstitial nephritis)*
    - **RBC casts** in AGN *(acute glomerulonephritis)*
  - Hansel stain for Eosinophils

NB

- **Urinalysis can differentiate between Different etiology**.
  - If the cause is pre-renal, the kidneys still normal so you will not find any abnormality in the urine unless if the pre-renal stay until it progress to the renal.
  - If it is renal:

    > Glomerular, you will find RBCs cast *(in the normal persons, you will find hyaline cast secreted from the tubules, and if the RBCs go out from the glomeruli, as the pass from the tubules, they will attatch to these proteins forming a cast indicating glumerular disease)*. So, when you see RBCs alone it is not specific.

    > Interstitial disease, you will find a lot of WBCs *(WBCs cast)*, and if there is WBCs it will be interstitial or pylonephritis.

    > Tubular damage, you will find the urine muddy brown. *(Coarse granular muddy brown cast)*

– Urinary Indices;*(fractional excretion of Na)*

$$FENa = \frac{U_{Na} \times P_{Cr}}{U_{Cr} \times P_{Na}} \times 100$$

- FENa < 1% (Pre-renal state). **MCQ**
  - May be *low* in selected intrinsic cause
    - Contrast nephropathy
    - Acute GN
    - Myoglobin induced ATN

- FENa > 1% (Intrinsic cause of ARF).

– Laboratory Evaluation:

- S_{Cr} *(serum creatinine)*, More reliable marker of GFR:
  - Falsely elevated with Septra, Cimetidine *(because they block the reabsorbtion of creatinine in the renal tubules ⇒ mild elevation but not very high elevation)*
  - Small change reflects large change in GFR .

- BUN *(blood urea nitrogen)*, generally follows S_{Cr} increase.
  - Elevation may be independent of GFR *(in case of)*:
    - Steroids, GI Bleeding (reabsorbtion of urea, so the urea will be higher than creatinine), Catabolic state, hypovolemia

- BUN/Cr helpful in classifying cause of ARF
  - Ratio > 20:1 suggests pre-renal cause

Differentiation between Acute and Chronic Renal Failure:

NB

- When you take CBC and found hemoglobin is low, it is chronic.
  - Because of decreased production of hemopiotin, which lead to decrease production of RBCs and that will be obvious after 120 days, the age of RBCs, unless if the cause of ARF is the blood loss.

	Acute	***Chronic***
History	Short (days-week)	Long (month-years)
Haemoglobin concentration	Normal	Low
Renal size	Normal	Reduced
Renal osteodystrophy (related to vit.D)	Absent	Present
Peripheral neuropathy	Absent	Present
Serum Creatinine concentration (cannot differentiate)	Acute reversible increase	Chronic irreversible

TABLE 3-3. Laboratory Tests Useful in the Diagnosis of Acute Renal Failure

Test	Favors Prerenal Disease	Favors ATN
BUN/P_{cr} ratio	>20:1	10–15:1
Rise in P_{cr}	Variable rate of rise with downward fluctuations in some patients	Progressive increase of ≥0.5 mg/dL per day, particularly in oliguric patients
Urinalysis	Normal or near normal; hyaline casts may be seen but are not an abnormal finding	Many granular casts with renal tubular epithelial cells and epithelial cell casts
U_{osm}	>500 mosmol/kg	<350 mosmol/kg
U_{Na}	<20 meq/L	>40 meq/L
FE_{Na}	<1 percent	>2 percent

Causes of acute renal failure:

Differentiation between Pre-renal, renal and post-renal causes

Prerenal	***Renal***	***Postrenal***
» Hypovolaemia » Decreased active blood volume » Decreased cardiac output » Renovascular obstruction	» Acute tubular necrosis » Interstinal nephritis » Glomerular disease (acute glomerulonephritis) » Small vessel disease » Intrarenal vasoconstriction (in sepsis) » Tubular obstruction	» Bilateral ureteric obstruction » Unilateral ureteric obstruction » Bladder outflow obstruction

Acute Tubular Necrosis:

– Often result of renal ischaemia ⇒ death of tubular cells or direct toxic injury by endogenous chemicals such as myoglobin (from muscle ⇒ rhabdomyolysis)
– Integrity of tubule is destroyed, obstructions and back-leakage
– Most common cause of intrinsic cause of ARF
– Often multifactorial
– Ischemic ATN:
  ▪ Hypotension, sepsis, prolonged pre-renal state
– Nephrotoxic ATN:
  ▪ Contrast, Antibiotics, Heme proteins
– Diagnose by history, FENa (>2%)
– Sediment with coarse granular casts, RTE cells
– Treatment is supportive care.
  ▪ Maintenance of euvolemia (with judicious use of diuretics, I/V Fluid as necessary)
  ▪ Avoidance of hypotension
  ▪ Avoidance of nephrotoxic medications (including NSAIDs and ACE-I)
  ▪ Dialysis *(for few day and they will recover, because the tubular cells will regenerate in a week or so)* , if necessary
– 80% will recover, if initial insult can be reversed

Contrast nephropathy :

NB

- When you give a contrast to susceptible pts with chronic kidney disease, hypovolemia or congestive heart failure, they may develop contrast nephropathy.
  - It is defined by increased creatinine within 12-24hrs after the contrast injection.

- 12-24 hours post exposure, peaks in 3-5 days .
- Non-oliguric, FE Na <1% !!
  - **(Important)** *It behave like pre-renal although it is renal.*
- RX/Prevention
  - *For pts of high risk like diabetics, chronic kidney disease and congestive heart failure, give them IV fluid before and after the contrast*
  - ½ NS 1 cc/kg/hr 12 hours pre/post.
- Mucomyst 600 BID pre/post (4 doses).
- Risk Factors: CKD, Hypovolemia ,DM,CHF.

Rhabdomyolysis:

- Diagnose with ↑ serum CK (usually > 10,000), urine dipstick (+) for blood, without RBCs on microscopy, pigmented granular casts
  - *Diagnosed with increased serum creatinine + myoglobine in the urine.*
- *Causes either traumatic or non-traumatic*:
  - Common after trauma ("crush injuries"), seizures, burns, limb ischemia occasionally after IABP or cardiopulmonary bypass
- Treatment is largely supportive care (with IVF).,

Acute Glomerulonephritis:

- Rare in the hospitalized patient.
- Diagnose by history, hematuria, RBC casts, proteinuria *(usually non-nephrotic range)*, low serum complement in post-infectious GN, RPGN often associated with anti-GBM or ANCA .
- Usually will need to perform renal biopsy .

Atheroembolic ARF :

– Associated with emboli of fragments of atherosclerotic plaque from aorta and other large arteries.
– Diagnose by history, physical findings (evidence of other embolic phenomena-- CVA, ischemic digits, "blue toe" syndrome, etc), low serum C3 and C4, peripheral eosinophilia, eosinophiluria, rarely WBC casts
– Commonly occur after intravascular procedures or cannulation (cardiac cath, CABG, AAA repair, etc.)

Acute Interstitial Nephritis:

– Usually drug induced.
– Methicillin, rifampin, NSAIDS.
– Develops 3-7 days after exposure.
– Fever, Rash , and eosinophilia common.
– U/A reveals WBC, WBC casts, + Hansel stain.
– Often resolves spontaneously.
– Steroids may be beneficial (if S_{Cr}>2.5 mg/dl)

- Changes during acute renal failure:

– Hyperkalaemia ($\Rightarrow$ ECG abnormalities)
– decreased bicarbonate
– elevated urea
– elevated creatinine
– elevated uric acid
– Hypocalcaemia
– Hyperphoshataemia

» In many chases kidney can recover from acute renal failure.

» The function has to be temporarily replaced by dialysis .

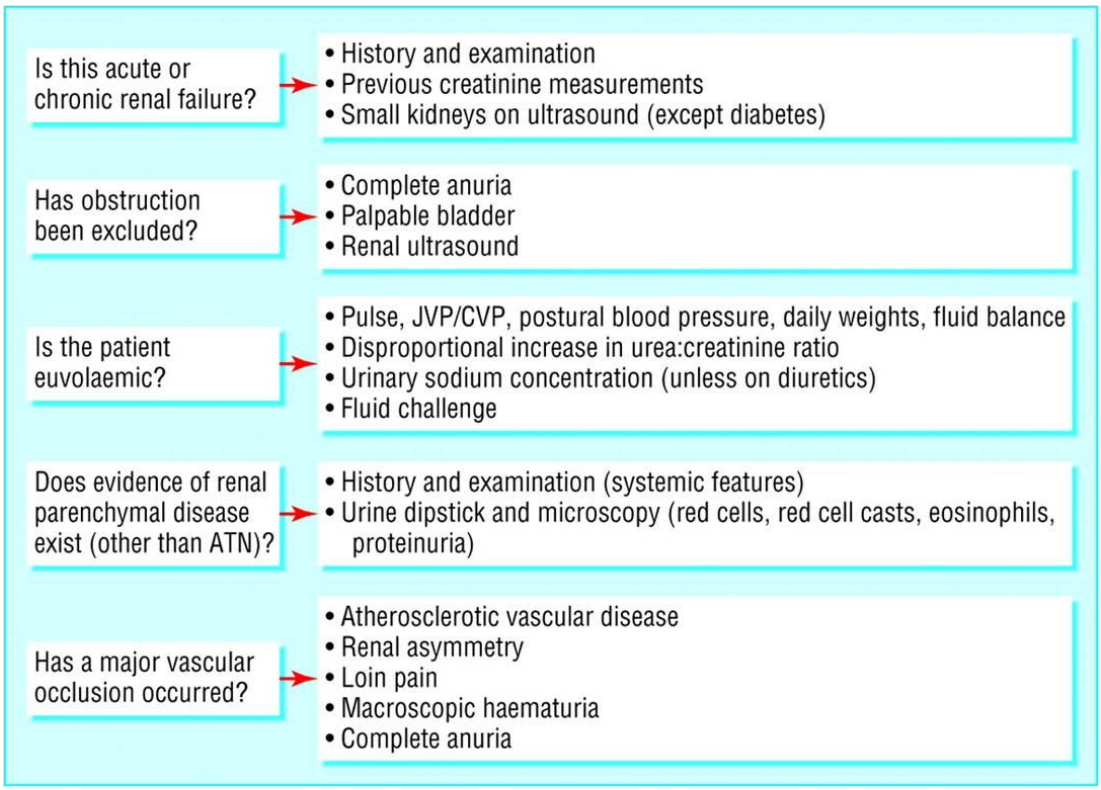
» Disturbed fluid or electrolyte homeostasis must be balanced.

» Primary causes like necrosis, intoxication or obstruction must be treated.

- Treatment of AKI (ARF):
  - Optimization of hemodynamic and volume status.
  - Avoidance of further renal insults (*damage by drugs, hypotension, ...)*
  - Optimization of nutrition.
  - If necessary, institution of renal replacement therapy.

- Indication for renal replacement therapy:
  - Symptoms of uremia (encephalopathy,...)
  - Uremic pericarditis
  - Refractory volume over load
  - Refractory hyperkalemia
  - Refractory metabolic acidosis

- Differential diagnosis of acute renal failure:



CASES:

Case-1

» 63 yrs. old women with Hx of long standing:
  - DM II and HTN (20 years)

» C/O: Muscle aches and pain for 2 weeks
  - No Hx of nausea, vomiting and diarrhea
  - Seen 3 days before at private clinic
  - Scr 139 *(normal is around 80)* ALT 160 *(normal is 40)* AST 83 U/A +3 glucose, +1 protein

» Medications list:
  - Bisoprolol *(β blocker)*, Irbesartan *(ARB)*, Simvasatin, and Gemfiborzil

» On Ex:
  - ill looking, Bp 140/90, P =105/min, O2 sat 95% on room air, JVP 3-4 cm ASA *(above sternal angle)*
  - No L.L oedema
  - Muscle tenderness with normal power
  - Chest: normal
  - CVS : normal S1 and S2 no murmurs

» Scr 350 *(before 3days, it was 139)*
» CK very high
» K =5.2
» U/A +3 protein,+3 Hb
» U/S kidney

Is this acute renal failure ? YES

What could be the reason for the ARF?

» Not pre-renal because the BP is OK and no history of pre-renal.
» Could be renal or post-renal, and by folly cath., we role out obstruction. So, we left with renal (tubular, interstitial, vascular or glomerular)
» There was no RBCs or RBCs cast – not glomerular
» She has hemoglobin – *muddy brown urine* – tubular (ATN)
  - Could be ischemic or toxic.
  - She doesn't have hypotension, so it is toxic.
  - She is on semvastatin and fibrate – so, **She Developed Rhabdomyolysis .**

Diagnosis and Treatment

» Supportive and dialysis for one or two times and stop the fibrate and statin and she will be ok.

Case -2

» 70 years old male
» C/O Vomiting blood for 1 day
» On Ex:
  - Bp 120/80 mmHg ,P=100/min JVP 4cm
» Lab:
  - Scr 80, urea 11*(normal is 4.5)*
» **Diagnosis?**
  - GI bleed can cause increase urea and if you treat it, he will be fine.

- Pre-renal AKI
  - History:
  - Physical examination
    - Volume status
      - Blood pressure, Pulse, JVP
      - Urine out put
  - Investigation:
    - Scr, urea
    - Urine analysis
    - Urine electrolytes

.: The End :.

Done By : *Nephro Team*

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